

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
ACID YELLOW 23

Chemical Code # 002155, Tolerance # 50316
SB 950 # 307
Original date: January 25, 2002

I. DATA GAP STATUS

Combined Chronic/Onco, rat:	Data gap, inadequate studies, no adverse effect indicated
Chronic toxicity, dog:	Data gap, inadequate study, no adverse effect indicated
Oncogenicity, mouse:	Data gap, no study on file
Reproduction, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rabbit:	Data gap, inadequate study, no adverse effect indicated
Gene mutation:	Data gap, no study on file
Chromosome effects:	Data gap, no study on file
DNA damage:	Data gap, no study on file
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 113566 in volume 50136 - 001 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T020125

Original: Kishiyama and Gee, January 25, 2002

Acid Yellow 23 and FD&C No. 5 are equivalent (Merck Index). Another name in the literature is tartrazine.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

50316 - 001 113563 A. C. Kahn III, Nair, K-P, Spicer, E. J. F. and Thorstenson, J. H. "Long-Term Dietary Toxicity/Carcinogenicity Study in Rats (114-Week Interim Report)." (International Research and Development Corporation, 410-003, June 26, 1980.) FD & C Yellow #5 Powder (lot AA3639, 90%) was fed at concentrations of 0.1, 1.0, or 2% in the diet throughout a long-term feeding study to 70 Charles River CD[®] rats/sex/group, beginning *in utero* as the F1 litters. Mean compound intake: males, 0, 48, 492 and 985 mg/kg/day; females, 0, 58, 590 and 1227 mg/kg/day. Hematology, clinical chemistry, urinalysis and ophthalmology were conducted at intervals during the study, with no clear treatment effects reported. 10/sex/group were sacrificed at 12 months. All tables and appendices are missing from the report, precluding independent evaluation of the study. From the summary report, hair, skin, urine and feces showed color changes in all FD&C Yellow #5 treatment groups, with color diminishing by week 22 at 0.1% diet. Histopathology data from the final sacrifice were not discussed in the interim report. NOEL not determined based on coloration at all doses. NOEL possibly \geq 2% of the diet based on lack of other findings as discussed in the 22-page report. UNACCEPTABLE (no tables or appendices were submitted, histopathological findings of the terminal sacrifice and second year deaths were not discussed). Possibly upgradeable if the complete final report, including the terminal sacrifice data, is submitted. (Kishiyama and Gee, 1/23/02).

50316 - 001 113566 Davis, K. J., O. G. Fitzhugh and A. A. Nelson. "Chronic Rat and Dog Toxicity Studies on Tartrazine". (FDA, published in *Toxicology and Applied Pharmacology* 6 (5): 621-626 (September 1964)). FD & C Yellow No. 5 (no purity stated) was admixed with the feed at concentrations of 0, 0.5, 1, 2, or 5% and fed for two years to 12 Osborne-Mendel rats/sex/group. Rats in the 5 and 2% groups experienced diarrhea, incidence not reported. Small amounts of whitish-tan gritty material were found in the renal pelvis of one 1% and three 5% male rats and regarded by the authors as possibly significant. The incidence of nephritis was not dose-related in incidence or severity. The incidence of tumors was not treatment-related. No worksheet. (Kishiyama and Gee, 1/23/02).

CHRONIC TOXICITY, DOG

50316 - 001 113566 Davis, K. J., O. G. Fitzhugh and A. A. Nelson. "Chronic Rat and Dog Toxicity Studies on Tartrazine". (FDA, published in *Toxicology and Applied Pharmacology* 6 (5): 621-626 (September 1964)). FD & C Yellow No. 5 was admixed with the feed at concentrations of 0, 1, or 2% of the diet and fed for two years to two Beagle dogs/sex/group. Hematologic examinations were made periodically. At the end of 2 years, the dogs were sacrificed and histological exams performed. There were no clinical observations, hematology changes, of gross lesions due to tartrazine. The only data presented were organ weights. An incidence of pyloric gastritis in one high dose female

was considered an equivocal treatment related effect. No worksheet. (Kishiyama and Gee, 1/23/02).

ONCOGENICITY, MOUSE

No Study Submitted

REPRODUCTION, RAT

50315 001 903932 Two page Summary of a study entitled “Summary of 3-Generation Reproduction Study”. FD & C Yellow #5 was admixed with the feed at doses of 0.0, 7.5, 75.0, 225.0 or 750 mg/kg/day and fed to 3 generations of 10 male and 20 female Long-Evans rats/group. No adverse reproductive effects reported in the summary.. UNACCEPTABLE (A full study was requested for review). (N. L. Hughett; C. N. Aldous; 8/19/85).

TERATOLOGY, RAT

50315 001 903929 “Segment II Rat Teratology Study”. (Bio/dynamics Inc., Project No. 71R-719A.) FD&C Yellow #5 was administered via intubation at doses of 0, 100, 300 or 1000 mg/kg/day to sexually mature Long-Evans female rats/group during Days 6 through 15 of gestations. No reported toxicity to dams or pups at doses up to 1000 mg/kg/day. UNACCEPTABLE (Insufficient information. The full study was requested for review). (N. L. Hughett and C. N. Aldous; 8/19/85). [See 50316 - 001, 113560 below. Gee, 1/23/02]

50316 - 001 113560 E. J. Sabol [Smith, J. M, Director of Toxicology] “Segment II Rat Teratology Study”. (Bio/dynamics Inc., Project No. 71R-719A, 1971.) FD&C Yellow #5 was administered via intubation at doses of 0 (0.5% methylcellulose, 3 groups), 100, 300 or 1000 mg/kg/day, to 22-23 sexually mature Long-Evans female rats/group during days 6 through 15 of gestation. Trypan Blue, 30 mg/kg, was given subcutaneously on days 7 through 9 as a positive control. One third of the fetuses were given a visceral exam and 2/3, a skeletal exam. Effects with Trypan Blue were as expected. No maternal or fetal effects of FD&C Yellow #5 were reported in the summary data. All appendices were missing from the document. Maternal and Developmental NOEL = 1000 mg/kg/day. UNACCEPTABLE (appendices missing, no analytical data on dosing material for actual content, clarification of negative controls). No adverse effect reported in the summary document of 12 pages. Possibly upgradeable. (Kishiyama and Gee, 1/23/02).

TERATOLOGY, RABBIT

50315 001 903930 Two page Summary of Study entitled “Segment II Rabbit Teratology Study”. (Bio/dynamics Inc., Project No. 71R-721A.) FD & C Yellow #5 was administered via gavage at doses of 0 (0.5% methylcellulose), 100, 300 or 1000 mg/kg/day to 17 mated sexually mature female New Zealand White rabbits/group during gestation days 6 through 18. UNACCEPTABLE (a full study

was requested for review). (N. L. Hughett; C. N. Aldous, 8/19/85). [See review of 113565 below. Gee, 1/23/02]

50316 - 001 113565 Murchio, A. [J. M. Smith, Director of Toxicology] "Segment II Rabbit Teratology Study". (Bio/dynamics Inc., Project No. 71R-721A, 1971?) FD & C Yellow # 5 (batch CCIC-7, 92%) was administered via gavage at doses of 0 (0.5% methylcellulose, three groups), 100, 300 and 1000 mg/kg/day to 17 mated female New Zealand White rabbits/group during gestation days 6 through 18. Volumes of dosing suspension given were 1 ml/kg at the low dose, 3 ml/kg at 300 mg/kg, and 3.3 ml/kg three times daily at 1000 mg/kg/day (timing not stated). Five of 17 does died at the high dose, possibly related to the difficulty in dosing this volume 3X a day. At C-section, there were 35, 12, 9 and 8 does, control through high dose groups, respectively. Weight gain at 1000 mg/kg/day was lower than the cumulative controls (159.4 g versus 207.1 g, days 6 - 18) but was not statistically significant. The increase in mean number of resorptions at the low (2.2) and high (2.3) doses, compared to 0.8 in controls, was attributed to selected does. The positive control, thalidomide, gave the expected effects. Apparent maternal NOEL = 300 mg/kg/day (slightly lower body weight change, mortality). The reduced bodyweight of high-dose fetuses (32.63 g versus 35.51 for cumulative controls), although not statistically significant, and the higher fetal incidence of ossification variations (no details of location), may be treatment related. Apparent developmental NOEL = 300 mg/kg/day. No teratogenic effects. UNACCEPTABLE (all tables and appendices of data were missing from the report; no information of dosing material analysis). No adverse effects in the summary report. Possibly upgradeable. (Kishiyama and Gee, 1/23/02).

GENE MUTATION

No Study Submitted

CHROMOSOME EFFECTS

No Study Submitted

DNA DAMAGE

No Study Submitted

NEUROTOXICITY

Not required at this time.